REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks. Non-elected claims 5-6, 9-13, and 16-17 are hereby canceled. Thus, claims 1, 3-4, 7-8, 14-15, and 18-22 are pending. Claims 7 and 18-22 are under consideration. Claims 7 and 18-21 have been amended and claims 23 and 24 have been added to more specifically recite certain aspects of the invention. Support for these amendments may be found throughout the specification and claims as originally filed, and it is urged that the amendments do not constitute new matter. It should also be noted that the above amendments are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application.

Amendment to the Specification

The Cross-Reference to Related Applications section has been amended to remove reference to certain prior applications, thereby canceling any priority claim to the removed applications.

Information Disclosure Statement

Applicants note that Reference AF of the Information Disclosure Statement submitted August 6, 2001 was crossed through and was not initialed on the corresponding Form PTO-1449. The Action indicates that this reference was not considered, because it was not provided in the instant application, and Applicants did not identify which parent application contains a copy of the reference.

Applicants respectfully request that this reference be considered and made of record in the instant application and that Applicants are provided with a copy of Form PTO-1449 in which this reference is initialed. For the Examiner's convenience, Applicants have included a copy of the reference, El-Deiry, *Current Opinion in Oncology* 9(1), 79 (1997), and a copy of previously submitted Form PTO-1449.

Rejections Under 35 U.S.C. §§ 101 and 112, First Paragraph

Claims 7 and 18-22 stand rejected under 35 U.S.C. § 101 on the alleged basis that the claimed invention lacks patentable utility. Claims 7 and 18-22 also stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. More specifically, the Action alleges that the instant specification does not disclose a specific, substantial, and credible utility for any of the claimed polypeptides. Furthermore, the Action asserts that it is not evident that one of skill in the art would find a patentable utility for the claimed polypeptides to be readily apparent given the disclosure in the instant application. The Action further alleges that the instant specification does not teach the skilled artisan how to use the claimed invention.

Applicants respectfully traverse this ground of rejection and submit that the specification clearly discloses at least one specific, substantial, and credible utility of the claimed invention. More specifically, Applicants submit that the skilled artisan would readily appreciate that the claimed L200T polypeptides are useful, for example, in the stimulation of tumor-specific T lymphocytes, as described, *e.g.,* on page 104, lines 11-28. Applicants submit that the specification clearly indicates that the L200T antigen of SEQ ID NO:586 was identified, using T cell expression cloning methods to screen a lung tumor-derived cDNA library, as a tumor-associated polypeptide capable of stimulating tumor infiltrating lymphocytes (TILs) specifically associated with the lung tumor cells from which the library was generated (Example 8). Furthermore, Applicants submit that the specification further demonstrates that both the L200T antigen of SEQ ID NO:586 and the region corresponding to amino acid residues 35-50 of L200T, as set forth in SEQ ID NO:587, are capable of stimulating proliferation of the tumor-specific T lymphocytes (see, *e.g.,* page 131, lines 6-14 and page 133, lines 5-10). Thus, Applicants submit that the specification, as originally filed, discloses a specific, substantial, and credible utility for the claimed invention that would be immediately recognized by the skilled artisan, *e.g.,* the use of L200T polypeptides to stimulate proliferation of tumor-specific T cells. Applicants further submit that the skilled artisan would recognize and appreciate the utility of stimulating proliferation of tumor-specific T cells, *e.g.,* for the production of tumor-specific T cells for use in

the adoptive immunotherapy of lung cancer, as described in the instant specification, *e.g.*, on page 104, lines 11-28. In addition, Applicants submit that the instant specification adequately teaches the skilled artisan how to use the invention accordingly. Specifically, Applicants note that Example 8 teaches detailed methods for stimulating the proliferation of tumor-specific T lymphocytes using the claimed polypeptides.

Applicants further note that the courts have clearly established that patentable utility does not require a demonstration of clinical efficacy. Rather, as distinctly noted in the M.P.E.P., "[c]ourts have repeatedly found that the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides 'an immediate benefit to the public' and thus satisfies the utility requirement." M.P.E.P. 8th ed. § 2107.01 III. The Federal Circuit specifically recognized that "[u]sefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans." *In re Brana,* 51 F.3d 1560 (Fed. Cir. 1995). Indeed, the M.P.E.P. notes that "courts have found utility for therapeutic inventions despite the fact that an applicant is at a very early stage in the development of a pharmaceutical product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition. M.P.E.P. 8th ed. § 2107.01 III, *citing Cross v. Iizuka,* 753 F.2d 1040, 1051 (Fed. Cir. 1985). Applicants submit that the claimed invention clearly possesses at least one demonstrated utility that meets the established requirements of Section 101, this utility being the ability of the claimed polypeptides to stimulate proliferation of tumor-specific T lymphocytes.

Applicants respectfully request that the rejections under 35 U.S.C. §§ 101 and 112, first paragraph, be reconsidered and withdrawn in light of these remarks.

Rejection Under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 7 and 18-22 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. More specifically, the Action

alleged that the instant specification does not disclose all polypeptides that comprise the sequences mentioned in the claims and does not disclose any effects of additional or flanking sequences on the activity of the claimed polypeptides.

Applicants respectfully traverse this basis of rejection and submit that the claimed subject matter is adequately described in the instant specification and, thus, meets the requirements of 35 U.S.C. § 112, first paragraph.

As an initial matter, Applicants submit that the claimed invention is based upon Applicants' discovery that L200T polypeptides (SEQ ID Nos:586 and 587) are tumor specific T cell antigens capable of stimulating T cell proliferation. Applicants further submit that it is widely known and accepted in the art that the stimulation of a T cell that recognizes a particular antigen does not necessarily require that the stimulating polypeptide have the identical sequence as the antigen. Rather, it is well understood that T cells recognize fragments of antigens, which result from the antigen being processed by and presented on the surface of antigen presenting cells. Accordingly, T cells typically respond to one or more epitopes or fragments of an entire antigen. In addition, Applicants submit that one skilled in the art would recognize that the substitution, deletion, or addition of one or more amino acid residues of a T cell antigen could be made without significantly decreasing the antigen's ability to stimulate antigen-specific T cells. For example, the skilled artisan would recognize that if the change was made to a non-epitope region of the antigen, it would be largely irrelevant, since the antigen would undergo processing that would remove the altered sequence before presentation of the epitope to the T cell. Similarly, the skilled artisan would recognize that if the change involved a conservative substitution, it would likely not affect the ability of the T cell to bind and respond to an epitope within the antigen.

In addition, Applicants submit that under the Examination Guidelines set forth by the Patent and Trademark Office, the written description requirement for a claimed genus may be satisfied by the description of a representative number of species or the disclosure of relevant, identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112, ¶1, "Written Description" Requirement, 66 Fed. Reg. 1099, at 1106. Applicants note that the

Guidelines clearly provide that acceptable identifying characteristics include both sequence and binding affinity. *Id.* at 1110. In fact, the examples provided in the Guidelines of sufficiently detailed, relevant identifying characteristics that provide evidence that applicant was in possession of the claimed invention include, "complete or partial structure....functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of these characteristics." *Id.* at 1106.

Applicants submit that the instant specification discloses sufficient identifying characteristics for L200T-related polypeptides with at least 90% identity to the sequences of SEQ ID NOs:586 and 587, since it provides both a reference sequence, percent identity limitations, and the functional limitation that the claimed polypeptides stimulate T cells specific for a polypeptide having the amino acid sequence of SEQ ID NO:586. Applicants submit that the identified sequence and functional characteristics of the claimed polypeptides clearly demonstrate that Applicants were in possession of the claimed polypeptides. Applicants also submit that the characteristic of having at least 90% identity to the sequence of SEQ ID NO:586 or SEQ ID NO:587 is undeniably a partial structure, which is acknowledged in the Guidelines as being a sufficient, relevant identifying characteristic. In addition, Applicants submit that this structural characteristic, particularly when coupled with the functional characteristic of stimulating T cells specific for a polypeptide having the amino acid sequence of SEQ ID NO:586, clearly establishes that Applicants were in possession of the claimed invention.

Furthermore, Applicants submit that the instant specification, by providing the sequences of SEQ ID NOs:586 and 587 and requiring that the claimed variants have at least 90% identity to said sequences, effectively describes a representative number of species, so as to satisfy the written description requirement. Applicants further submit that the claimed genus of L200T polypeptide variants having at least 90% identity to SEQ ID NO:586 or SEQ ID NO:587 includes a limited number of species, which could be readily predicted and identified by the skilled artisan based upon the provided sequences. Applicants note that the Guidelines explicitly state that "[a] 'representative number of species' means that the species which are adequately described are representative of the entire genus" and that "there may be situations where one species adequately supports a genus." *Id.* at 1106. The Guidelines further note that "satisfactory

disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed" and that "[d]escription of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces." *Id.* Applicants submit that the skilled artisan would clearly recognize that Applicants were in possession of the claimed genus based upon the disclosure of the polypeptide sequences of SEQ ID NOs:586 and 587, particularly in light of the associated percent identity and functional limitations and the clear appreciation in the art that the claimed polypeptide variants would be capable of stimulating a T cell specific for an L200T polypeptide.

In addition, Applicants submit that the instant specification discloses sufficient identifying characteristics for L200T-related polypeptides comprising at least 10 contiguous residues of either SEQ ID NOs:586 and 587, since it provides both a reference sequence and the functional limitation that the claimed polypeptides stimulate T cells specific for a polypeptide having the amino acid sequence of SEQ ID NO:586. Applicants further note that the skilled artisan would readily appreciate that T cell epitopes may comprise as little as 10 amino acid residues of a corresponding antigen and that the identification of fragments having the claimed characteristics requires merely routine screening procedures that are widely known and available in the art. Furthermore, methods of screening L200T fragments for their ability to stimulate T cells specific for the L200T polypeptide of SEQ ID NO:586 are described in detail in the instant application and have been demonstrated to be successful in identifying L200T epitopes, including the epitope set forth in SEQ ID NO:587 (see, *e.g.*, Example 8).

In light of these remarks, Applicants submit that the instant claims satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, and respectfully request that this basis of rejection be reconsidered and withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 7 and 18-22 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which

Applicants regards as the invention. More specifically, the Action asserts that (a) claims 19 and 20 are vague and indefinite in their recitation of "specific for," because the meaning of this term is unclear in the context of the claims, (b) claims 19 and 20 are vague and indefinite in the recitation of "having an amino acid sequence of SEQ ID NO:586," because it is not clear whether the claims require the entirety of SEQ ID NO:586, (c) claim 18 is vague and indefinite in its recitation of "an amino acid sequence set forth in SEQ ID NO:586," because it is not clear whether the claims require the entirety of SEQ ID NO:586, and (d) claim 21 is vague and indefinite in its recitation of "an amino acid sequence of claim 587," because it is not clear whether the claims require the entirety of SEQ ID NO:587. The Action indicates that the substitution of "the" for "an" would overcome this rejection as related to parts (b)-(d).

Applicants respectfully traverse this basis of rejection and submit that the skilled artisan would clearly understand the metes and bounds of the claimed invention, particularly in light of the teachings of the instant specification. Applicants first submit that the phrase "specific for," as used in the claims to refer to T cells specific for a particular antigen, is well-understood and widely accepted in the art, as evidenced by its common usage in immunology textbooks. For example, in the section entitled, "Lymphocyte Specificity and Activation," Abbas *et al.* describe "the fundamental concept that helper and cytolytic T lymphocytes **specific for** foreign protein antigens simultaneously recognize two structures, the foreign antigen and a self MHC molecule, both of which are present on the APC or target cell." *Cellular and Molecular Immunology,* W.B. Saunders Company, Philadeplphia, 1991, p. 120 (emphasis added). Similarly, in the chapter entitled, "T Lymphocyte Activation," Weiss refers to **antigen specific** responding T cells. *Fundamental Immunology,* Second Edition, W. E. Paul, ed., Raven Press, New York, 1989, p. 361. Applicants submit that the use of this term in these two widely used textbooks provides clear evidence that the skilled artisan would understand its meaning. In addition, Applicants note that T cells specific for a polypeptide of the invention are defined in the instant specification, e.g., on page 84, line 25 - page, 85, line 18. Accordingly, Applicants submit that the skilled artisan is well-apprised of the meaning of the term "specific for" in the context of the claimed invention.

Furthermore, Applicants note that claims 18-21 have been amended, as suggested by the Examiner and for the purpose of providing additional clarity, to recite "the" instead of "an." Applicants submit that the claims satisfy the requirements of Section 112, second paragraph, and respectfully request that this basis of rejection be withdrawn.

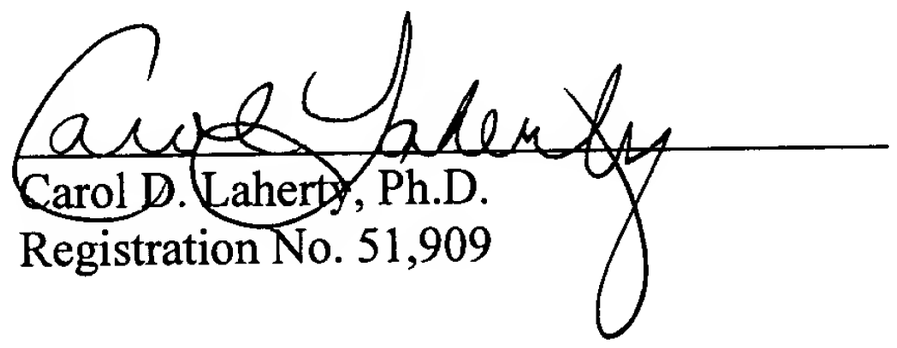
The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

It is respectfully submitted that all of the claims remaining in the application are believed to be allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Michael J. Lodes et al.

SEED Intellectual Property Law Group PLLC



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Enclosure:
Postcard
Copy of El-Deiry, *Current Opinion in Oncology* 9(1), 79 (1997)
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